

L35 ANSWER 191 OF 272 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1992:483431 HCAPLUS Full-text  
 DOCUMENT NUMBER: 117:83431  
 TITLE: Preparation of labeled cyclosporine derivatives for  
 immunoassay reagents and method for determining  
 cyclosporine  
 INVENTOR(S): Morrison, Marjorie A.; Meucci, Victoria P.; Lunetta,  
 Steven E.; Zajac, Mariola B.; Simpson, Elizabeth A.  
 PATENT ASSIGNEE(S): Abbott Laboratories, USA  
 SOURCE: Eur. Pat. Appl., 33 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 473961	A2	19920311	EP 1991-113328	19910808
EP 473961	A3	19930414		
EP 473961	B1	19960103		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE				
AT 132504	E	19960115	AT 1991-113328	19910808
ES 2084069	T3	19960501	ES 1991-113328	19910808
CA 2049089	AA	19920216	CA 1991-2049089	19910813
CA 2049089	C	20020903		
AU 9182471	A1	19920220	AU 1991-82471	19910814
AU 642035	B2	19931007		
JP 04253999	A2	19920909	JP 1991-205233	19910815
JP 3171460	B2	20010528		
US 5489668	A	19960206	US 1993-148164	19931104
US 5750413	A	19980512	US 1995-433104	19950504
PRIORITY APPLN. INFO.:			US 1990-567842	A 19900815

US 1992-952488

B1 19920928

US 1993-148164

A3 19931104

OTHER SOURCE(S): MARPAT 117:83431

AB Cyclosporine (I) derivs. useful as detectable tracer compds. for the immunochem. determination of I are disclosed. The I derivs. (Markush included) comprise a detectable moiety coupled to the amino acid of the 1st, 2nd, 3rd, 8th, or 10th position in I. A preferred derivative comprises a fluorescent moiety coupled to the OH group of the amino acid at the 1st position of I, and is especially useful for determination of I by fluorescence polarization immunoassay. A related method and kit are also disclosed. Preparation of a variety of fluorescein derivative-labeled I derivs. is described. A fluorescence polarization immunoassay protocol for I determination in e.g. serum is also described; a standard curve (0-400 ng I/mL) is included.

IT 63556-16-1P 141656-62-4P 141749-38-4P  
 141749-42-0P 141749-43-1P 141749-60-2P  
 141749-70-4P 141749-71-5P 141749-72-6P  
 141749-73-7P 141749-75-9P 141749-76-0P  
 141769-13-3P 141769-15-5P 141769-17-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, for detectably labeled cyclosporine derivative preparation)

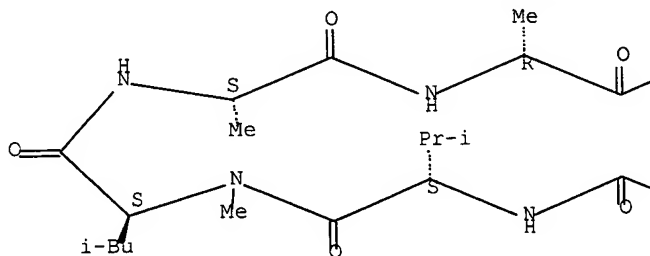
RN 63556-16-1 HCAPLUS

CN Cyclosporin A, 7-L-threonine-, 7-acetate (9CI) (CA INDEX NAME)

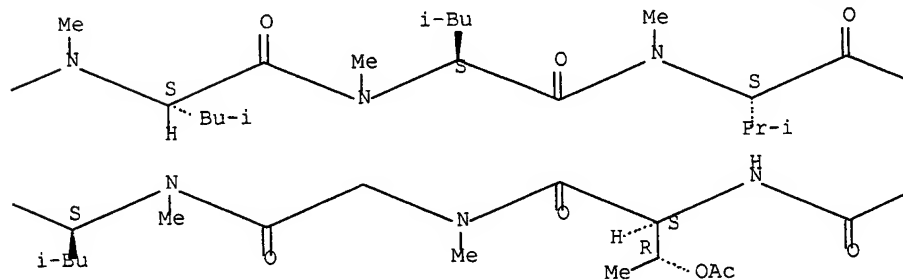
Absolute stereochemistry. Rotation (-).

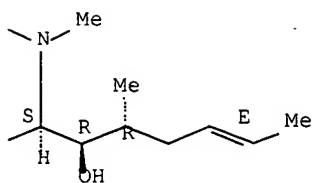
Double bond geometry as shown.

PAGE 1-A

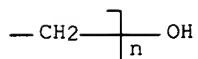
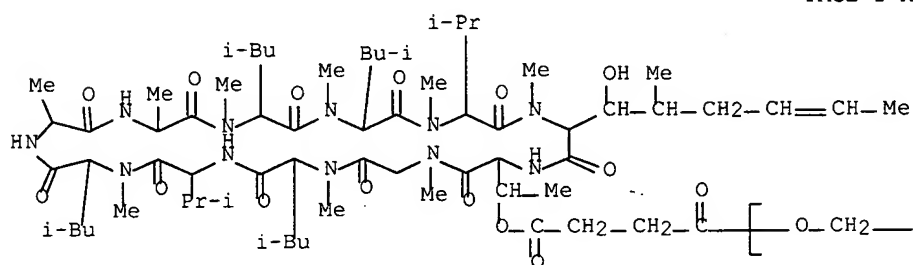


PAGE 1-B





RN 141656-62-4 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -(3-carboxy-1-oxopropyl)- $\omega$ -hydroxy-  
, 7-ester with 7-L-threoninecyclosporin A (9CI) (CA INDEX NAME)

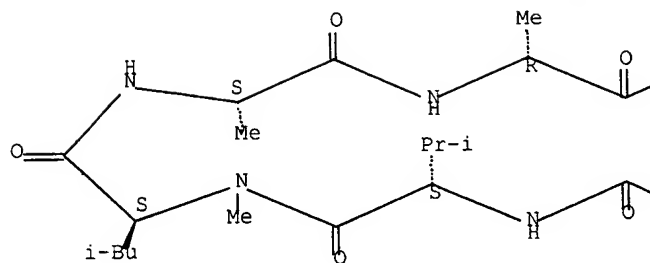
RN 141749-38-4 HCAPLUS

CN Cyclosporin A, carbonochloridate (ester) (9CI) (CA INDEX NAME)

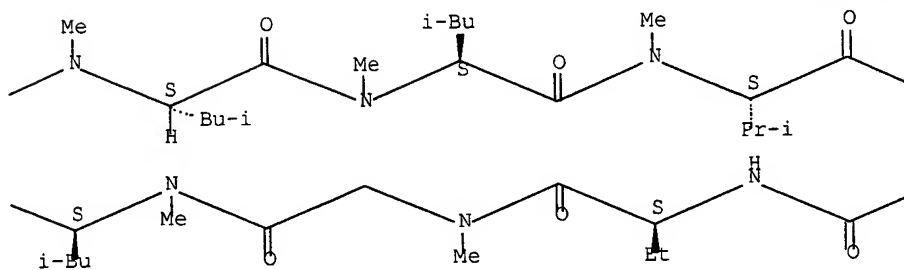
Absolute stereochemistry.

Double bond geometry as shown.

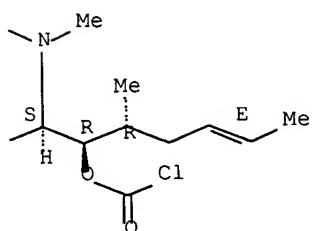
PAGE 1-A



PAGE 1-B



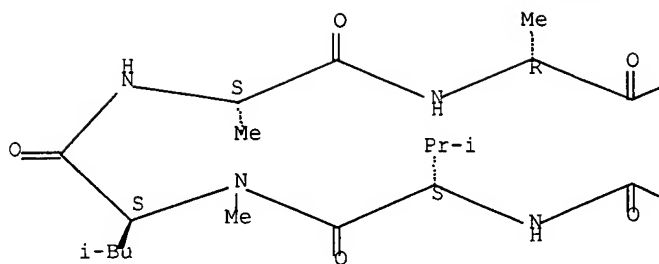
PAGE 1-C



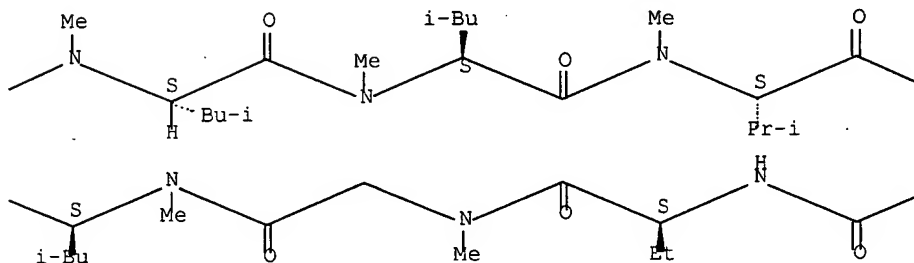
RN 141749-42-0 HCAPLUS  
 CN Cyclosporin A, chloroacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

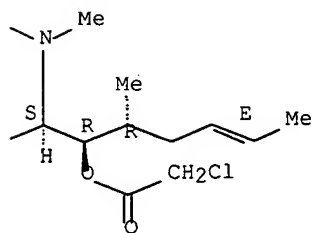
PAGE 1-A



PAGE 1-B



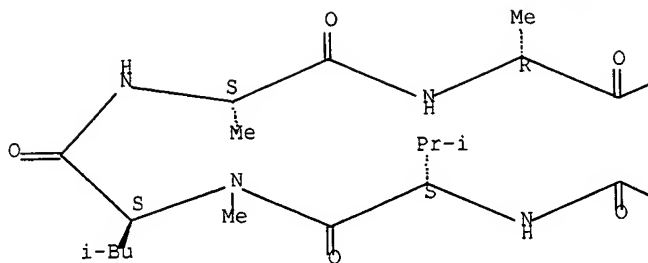
PAGE 1-C



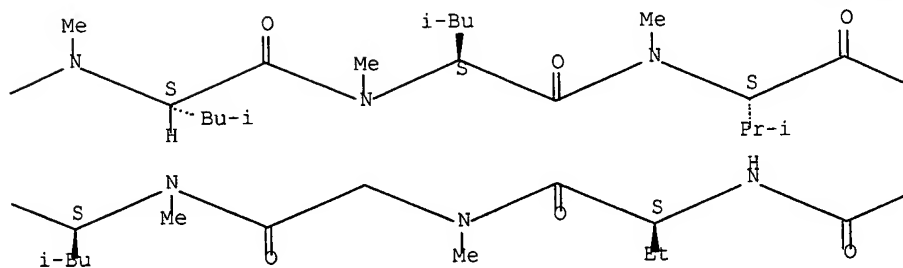
RN 141749-43-1 HCAPLUS  
 CN Cyclosporin A, ester with glycine (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

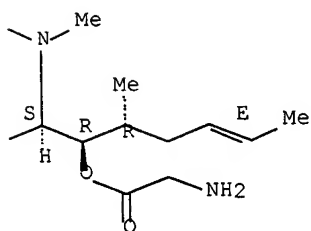
PAGE 1-A



PAGE 1-B

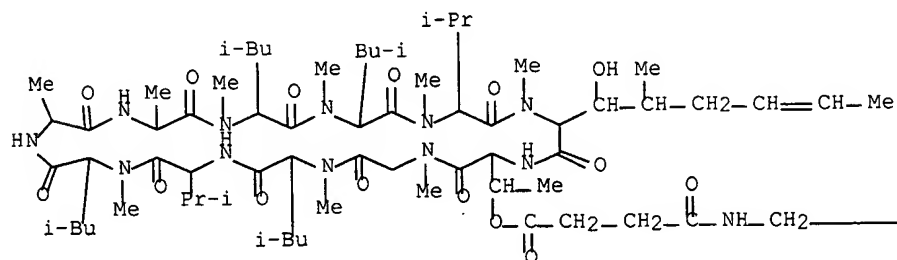


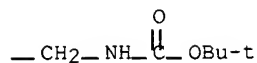
PAGE 1-C



RN 141749-60-2 HCAPLUS  
CN Cyclosporin A, 7-[O-[4-[[2-[[[(1,1-dimethylethoxy)carbonyl]amino]ethyl]amin  
o]-1,4-dioxobutyl]-L-threonine]- (9CI) (CA INDEX NAME)

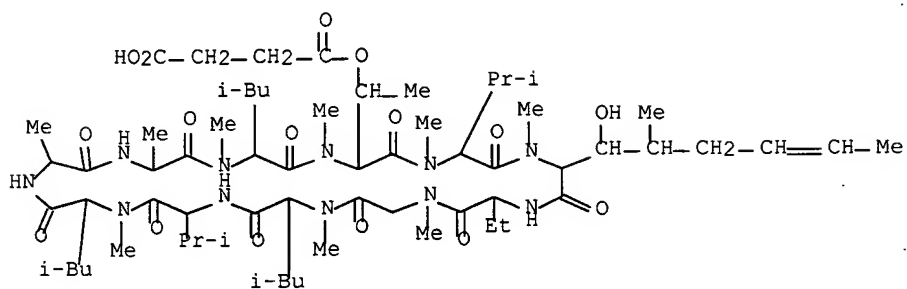
PAGE 1-A





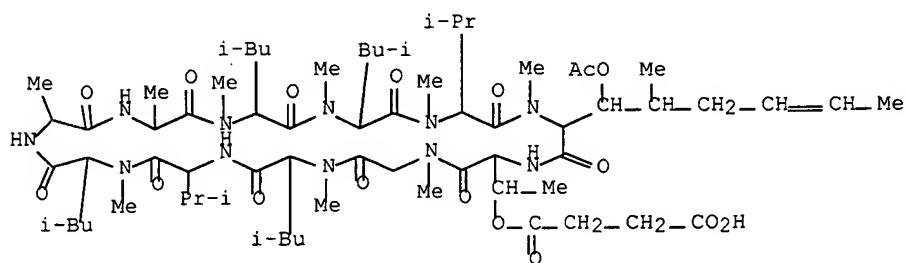
RN 141749-70-4 HCAPLUS

CN Cyclosporin A, 4-[O-(3-carboxy-1-oxopropyl)-N-methyl-L-threonine]- (9CI)  
(CA INDEX NAME)



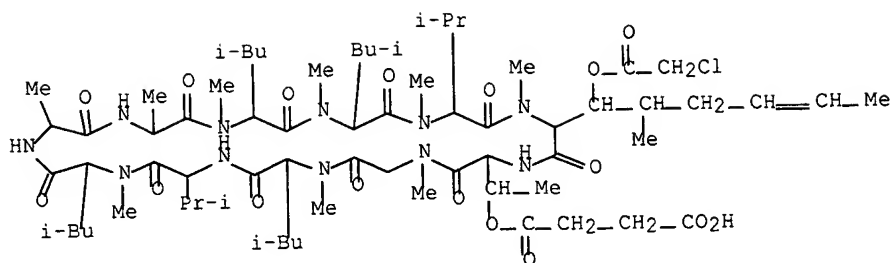
RN 141749-71-5 HCAPLUS

CN Cyclosporin A, 7-[O-(3-carboxy-1-oxopropyl)-L-threonine]-, acetate (ester)  
(9CI) (CA INDEX NAME)

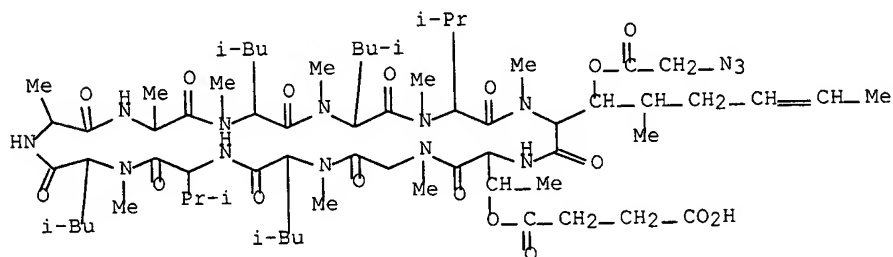


RN 141749-72-6 HCAPLUS

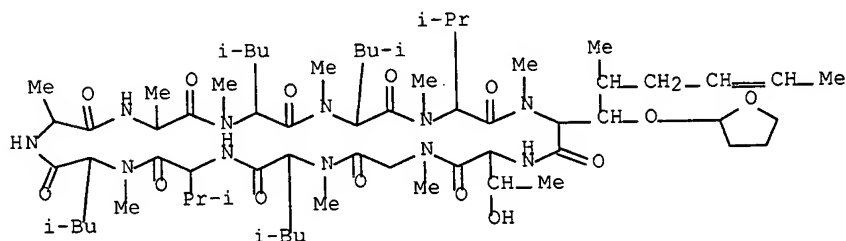
CN Cyclosporin A, 7-[O-(3-carboxy-1-oxopropyl)-L-threonine]-, chloroacetate  
(ester) (9CI) (CA INDEX NAME)



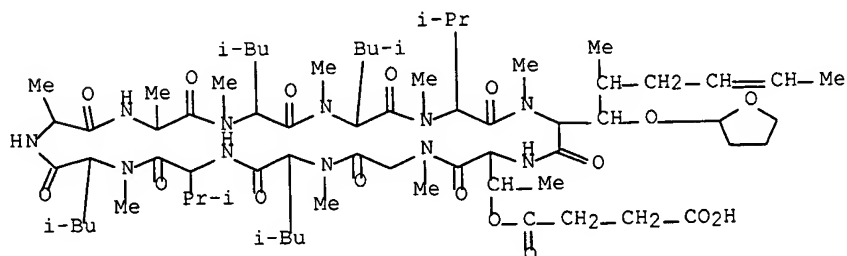
RN 141749-73-7 HCAPLUS  
 CN Cyclosporin A, 7-[O-(3-carboxy-1-oxopropyl)-L-threonine]-, azidoacetate (ester) (9CI) (CA INDEX NAME)



RN 141749-75-9 HCAPLUS  
 CN Cyclosporin A, 6-[(3R,4R,6E)-6,7-didehydro-N,4-dimethyl-3-[(tetrahydro-2-furanyl)oxy]-L-2-aminooctanoic acid]-7-L-threonine- (9CI) (CA INDEX NAME)

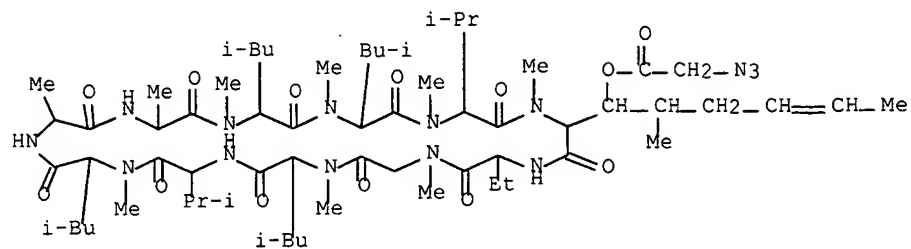


RN 141749-76-0 HCAPLUS  
 CN Cyclosporin A, 6-[(3R,4R,6E)-6,7-didehydro-N,4-dimethyl-3-[(tetrahydro-2-furanyl)oxy]-L-2-aminooctanoic acid]-7-[O-(3-carboxy-1-oxopropyl)-L-threonine]- (9CI) (CA INDEX NAME)

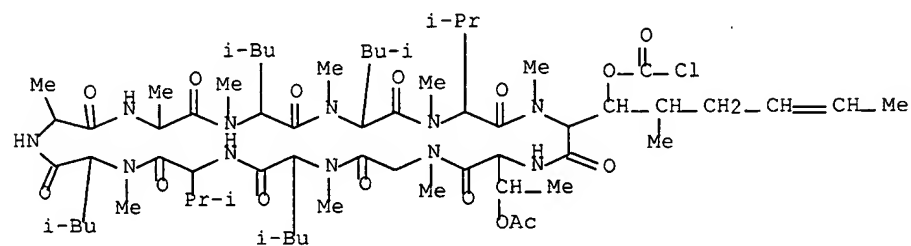




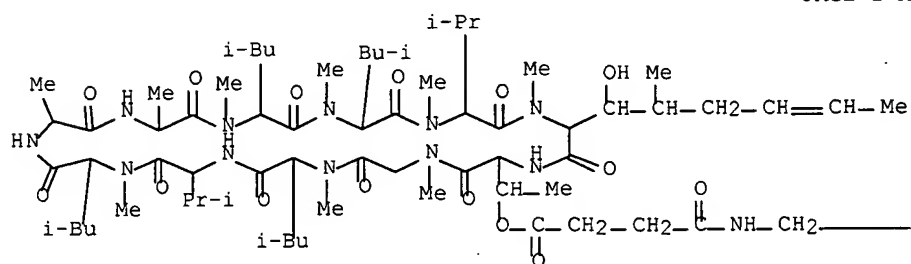
RN 141769-13-3 HCAPLUS  
 CN Cyclosporin A, azidoacetate (ester) (9CI) (CA INDEX NAME)



RN 141769-15-5 HCAPLUS  
 CN Cyclosporin A, 7-(O-acetyl-L-threonine)-, carbonochloridate (ester) (9CI)  
 (CA INDEX NAME)



RN 141769-17-7 HCAPLUS  
 CN Cyclosporin A, 7-[O-[4-[(2-aminoethyl)amino]-1,4-dioxobutyl]-L-threonine]-  
 (9CI) (CA INDEX NAME)



PAGE 1-A

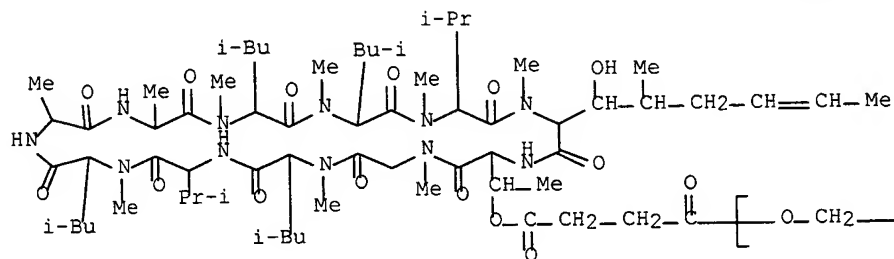
—CH<sub>2</sub>—NH<sub>2</sub>IT 141656-63-5PRL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, detectably labeled cyclosporine derivative preparation in relation to)

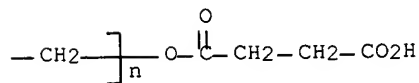
RN 141656-63-5 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -(3-carboxy-1-oxopropoxy)- $\omega$ -(3-carboxy-1-oxopropyl)-, 7-ester with 7-L-threoninecyclosporin A (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



IT 141656-61-3P 141749-37-3P 141749-39-5P  
141749-40-8P 141749-44-2P 141749-45-3P  
141749-46-4P 141749-48-6P 141749-50-0P  
141749-51-1P 141749-53-3P 141749-54-4P  
141749-56-6P 141749-58-8P 141749-59-9P  
141749-61-3P 141749-63-5P 141749-65-7P  
141749-67-9P 141749-69-1P 141749-74-8P  
141749-77-1P 141749-78-2P 141749-79-3P  
141769-14-4P 141769-16-6P 141769-18-8P  
141769-19-9P 141769-21-3P 141769-22-4P  
142064-94-6P 142123-01-1P

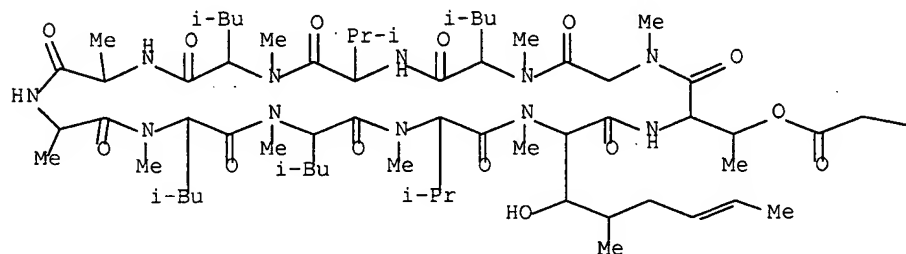
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, for cyclosporine immunoassay)

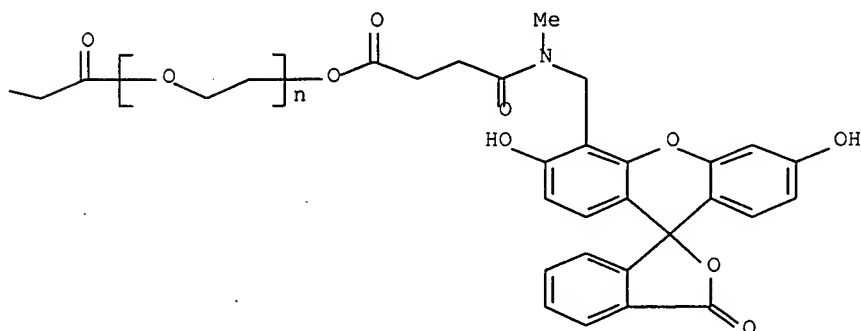
RN 141656-61-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -(3-carboxy-1-oxopropoxy)- $\omega$ -[4-  
[[ (3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-4'-  
yl)methyl]methylamino]-1,4-dioxobutoxy]-, 7-ester with  
7-L-threoninecyclosporin A (9CI) (CA INDEX NAME)

PAGE 1-A



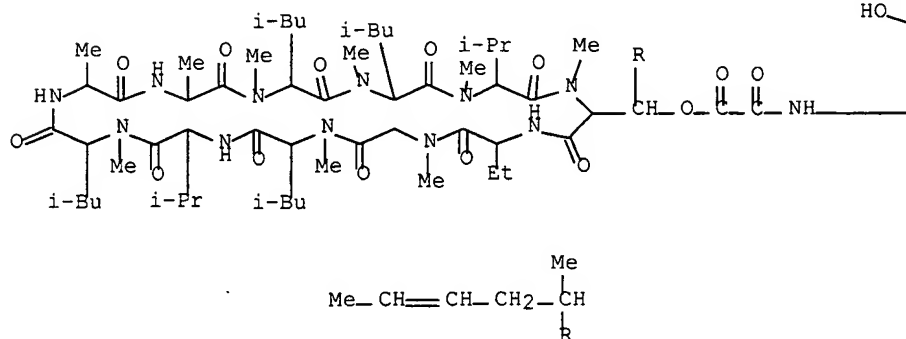
PAGE 1-B

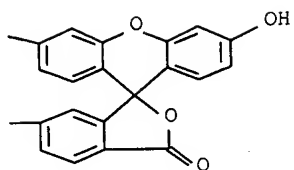


RN 141749-37-3 HCAPLUS

CN Cyclosporin A, [(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-  
[9H]xanthen]-6-yl)amino]oxoacetate (ester) (9CI) (CA INDEX NAME)

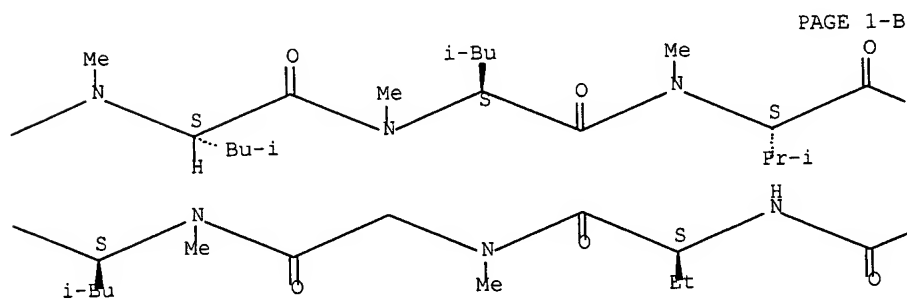
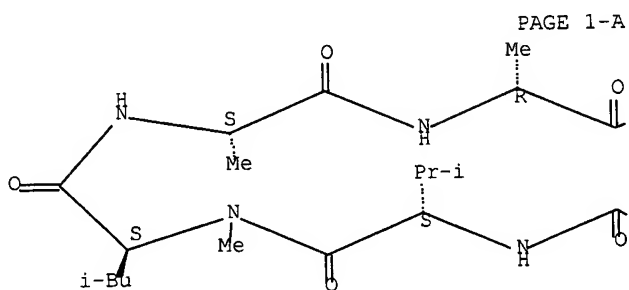
PAGE 1-A

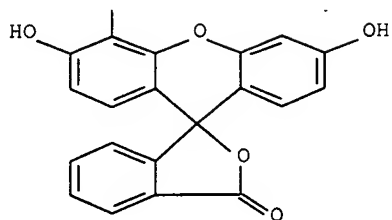
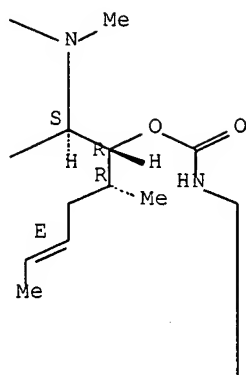




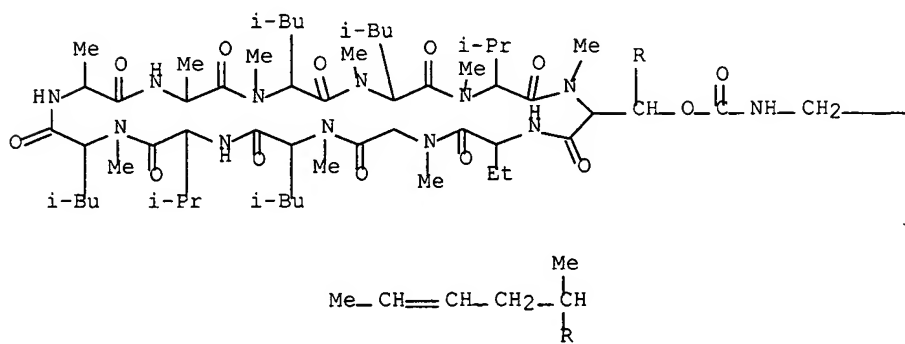
RN 141749-39-5 HCAPLUS  
 CN Cyclosporin A, [(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-4'-yl)methyl]carbamate (ester) (9CI) (CA INDEX NAME)

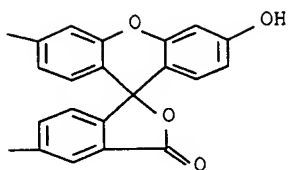
Absolute stereochemistry.  
 Double bond geometry as shown.



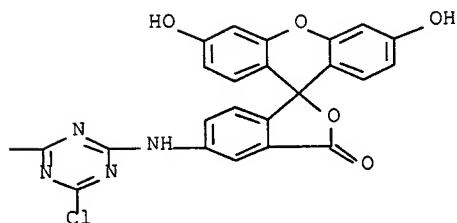
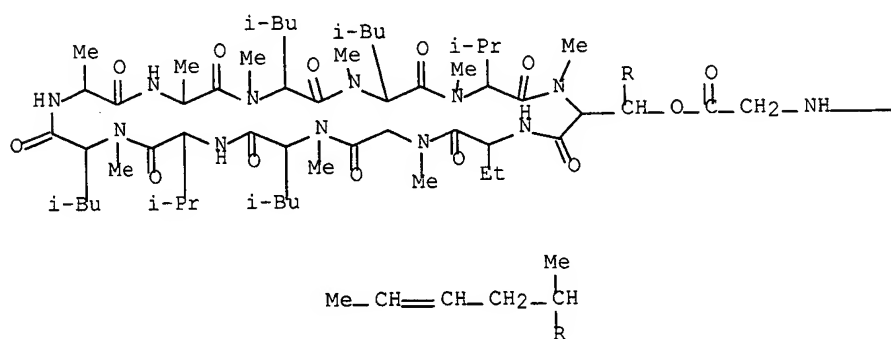


RN 141749-40-8 HCAPLUS  
 CN Cyclosporin A, [(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-6-yl)methyl]carbamate (ester) (9CI) (CA INDEX NAME)



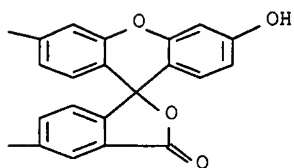
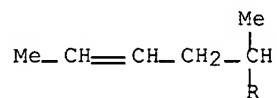
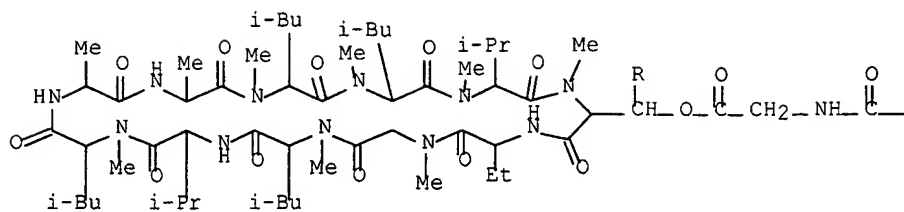


RN 141749-44-2 HCAPLUS  
 CN Cyclosporin A, ester with N-[4-chloro-6-[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-6-yl)amino]-1,3,5-triazin-2-yl]glycine (9CI) (CA INDEX NAME)



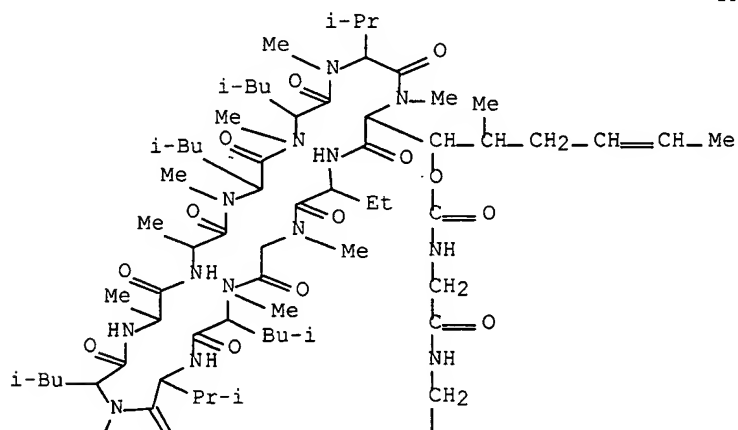
RN 141749-45-3 HCAPLUS  
 CN Cyclosporin A, ester with N-(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-6-yl)glycine (9CI) (CA INDEX NAME)

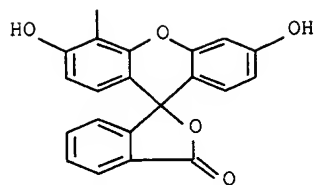
HO—



RN 141749-46-4 HCAPLUS

CN Cyclosporin A, [2-[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-4'-yl)amino]-2-oxoethyl]carbamate (ester) (9CI) (CA INDEX NAME)

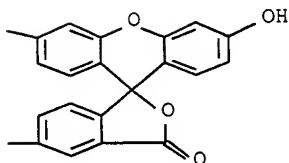
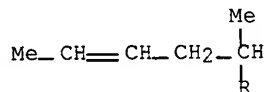
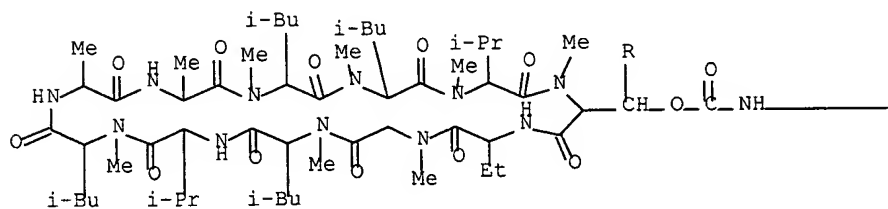




RN 141749-48-6 HCAPLUS

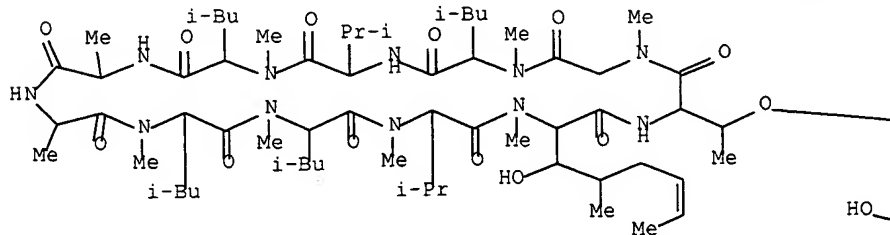
CN Cyclosporin A, (3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-6-yl)carbamate (ester) (9CI) (CA INDEX NAME)

HO-

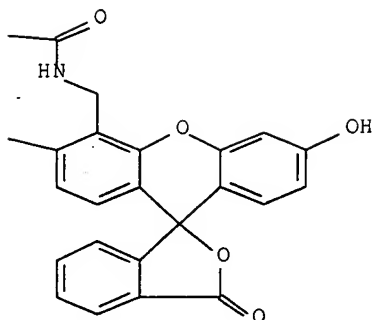


RN 141749-50-0 HCAPLUS

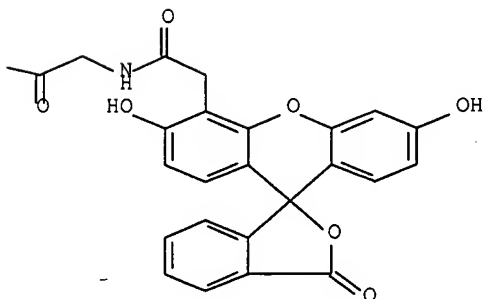
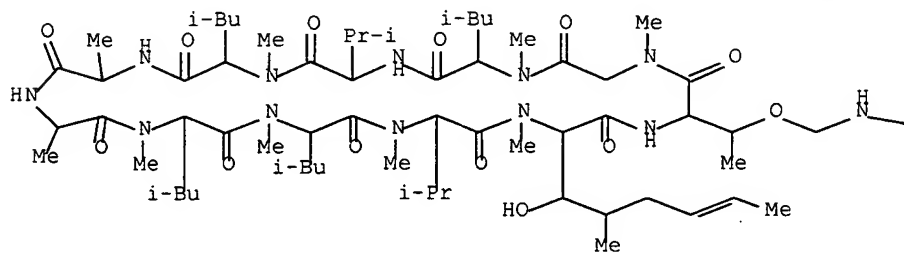
CN Cyclosporin A, 7-[O-[[[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-4'-yl)methyl]amino]carbonyl]-L-threonine]- (9CI) (CA INDEX NAME)







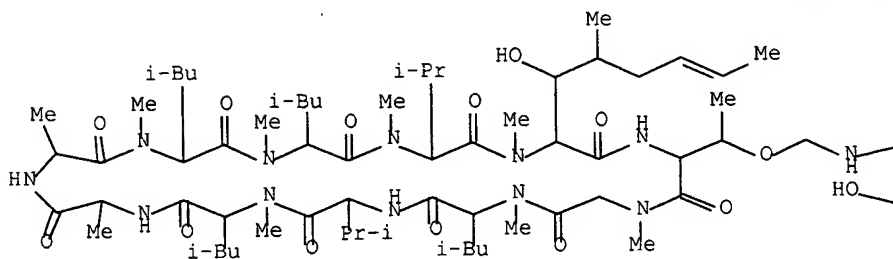
RN 141749-51-1 HCAPLUS  
 CN Cyclosporin A, 7-[O-[[[[[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-4'-yl)acetyl]amino]acetyl]amino]methyl]-L-threonine]-(9CI) (CA INDEX NAME)



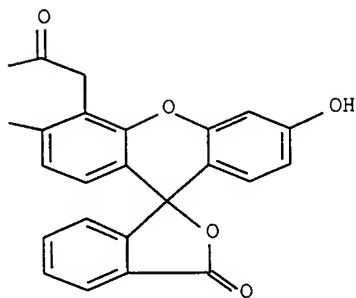
RN 141749-53-3 HCAPLUS

CN Cyclosporin A, 7-[O-[[[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-4'-yl)acetyl]amino]methyl]-L-threonine]- (9CI) (CA INDEX NAME)

PAGE 1-A



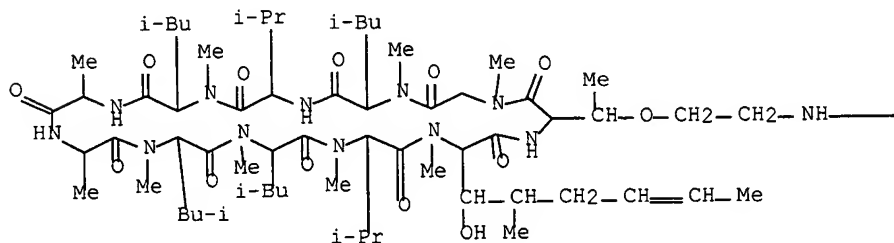
PAGE 1-B

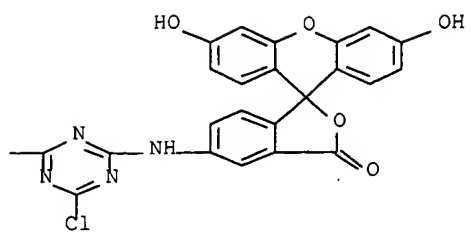


RN 141749-54-4 HCAPLUS

CN Cyclosporin A, 7-[O-[2-[[4-chloro-6-[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-6-yl)amino]-1,3,5-triazin-2-yl]amino]ethyl]-L-threonine]- (9CI) (CA INDEX NAME)

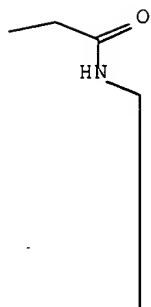
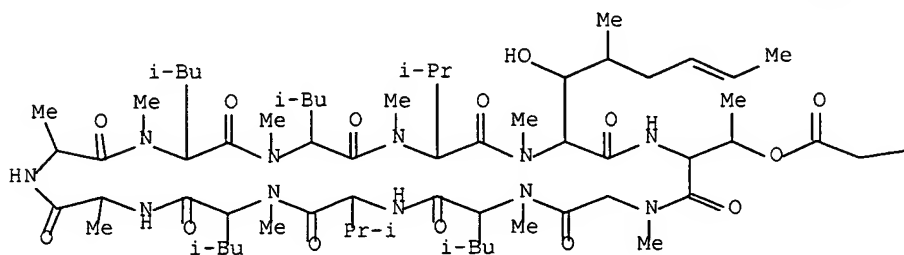
PAGE 1-A

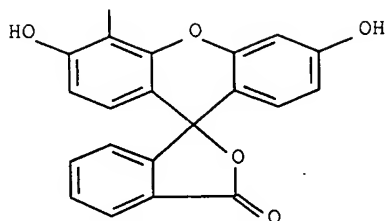




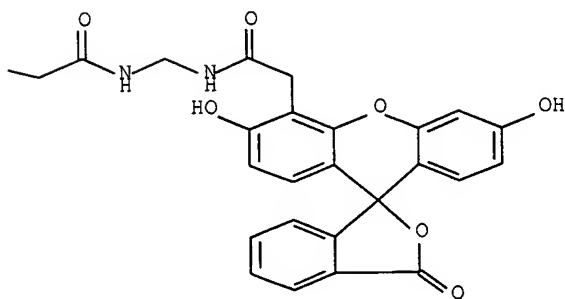
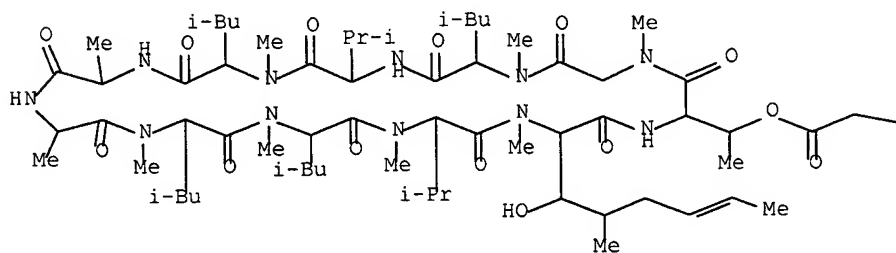
RN 141749-56-6 HCAPLUS

CN Cyclosporin A, 7-[O-[4-[[[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-4'-yl)methyl]amino]-1,4-dioxobutyl]-L-threonine]-(9CI) (CA INDEX NAME)

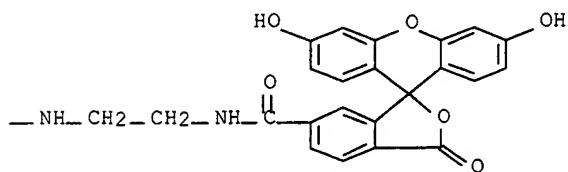
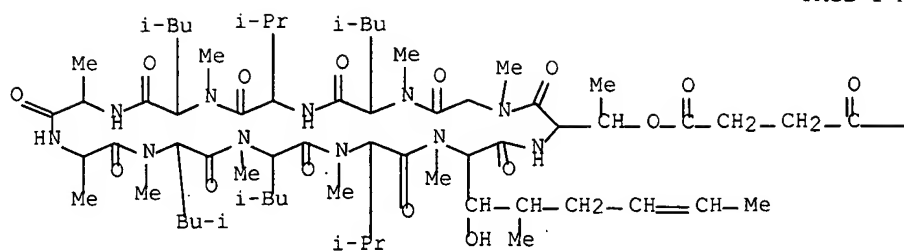




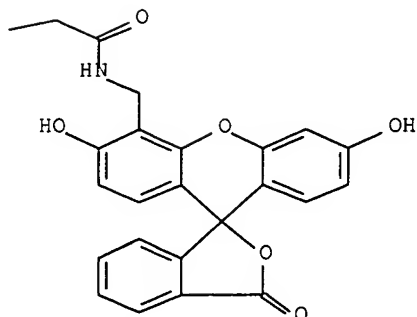
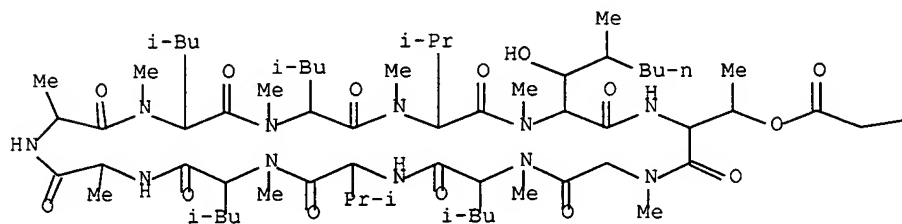
RN 141749-58-8 HCAPLUS  
 CN Cyclosporin A, 7-[O-[4-[[[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-4'-yl)carbonyl]amino]methyl]amino]-1,4-dioxobutyl]-L-threonine]- (9CI) (CA INDEX NAME)



RN 141749-59-9 HCAPLUS  
 CN Cyclosporin A, 7-[O-[4-[2-[[[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)carbonyl]amino]ethyl]amino]-1,4-dioxobutyl]-L-threonine]- (9CI) (CA INDEX NAME)

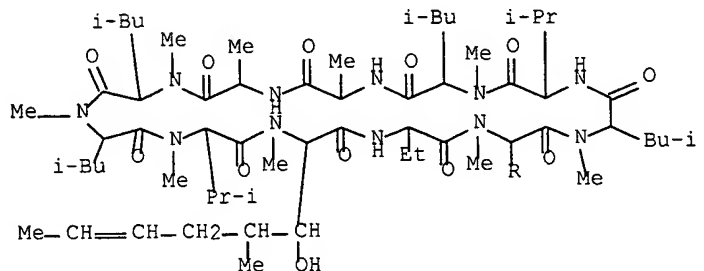


RN 141749-61-3 HCAPLUS  
 CN Cyclosporin A, 6-[(3R,4R)-3-hydroxy-N,4-dimethyl-L-2-aminooctanoic acid]-7-[O-[4-[[[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen)-4'-yl)methyl]amino]-1,4-dioxobutyl]-L-threonine]- (9CI) (CA INDEX NAME)

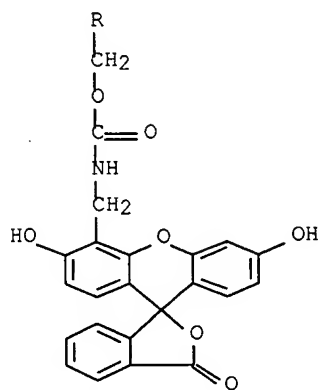


RN 141749-63-5 HCAPLUS  
 CN Cyclosporin A, 8-[O-[[[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen)-4'-yl)methyl]amino]carbonyl]-N-methyl-D-serine]- (9CI) (CA INDEX NAME)

PAGE 1-A

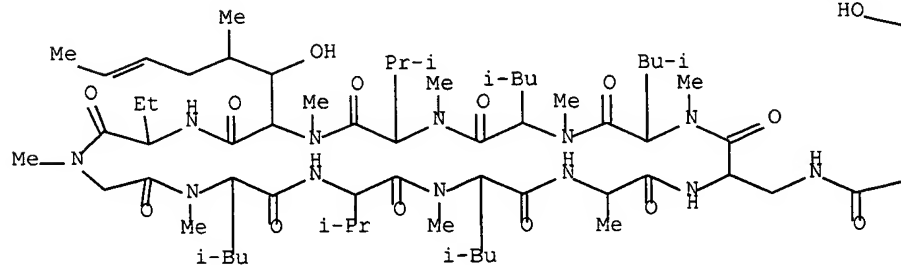


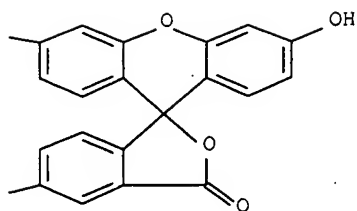
PAGE 2-A



RN 141749-65-7 HCAPLUS  
 CN Cyclosporin A, 2-[3-[[[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen)-6-yl]carbonyl]amino]-D-alanine]- (9CI) (CA INDEX NAME)

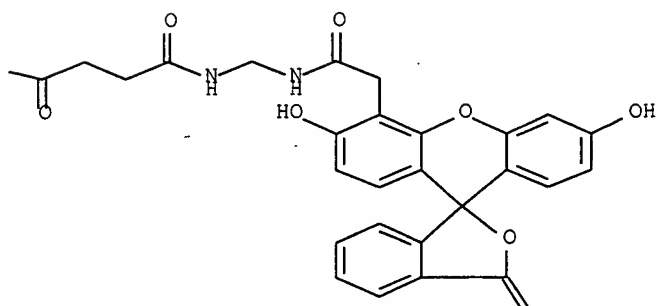
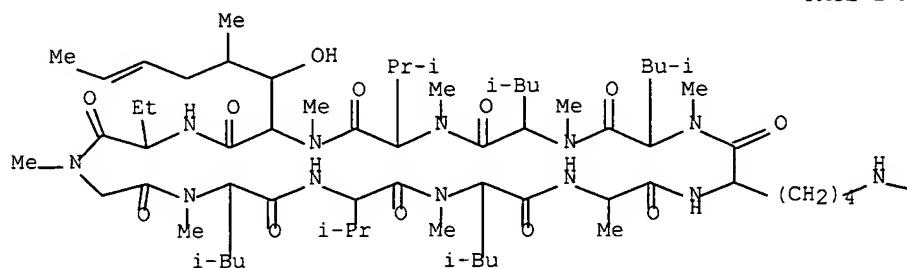
PAGE 1-A  
 HO—





RN 141749-67-9 HCAPLUS

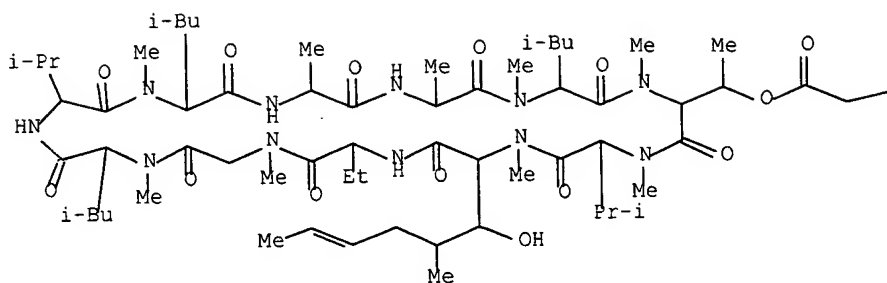
CN Cyclosporin A, 2-[N6-[4-[[[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-4'-yl)acetyl]amino]methyl]amino]-1,4-dioxobutyl]-D-lysine]- (9CI) (CA INDEX NAME)



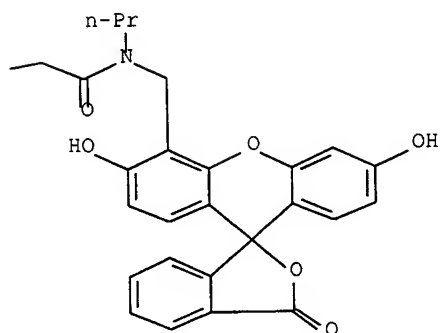
RN 141749-69-1 HCAPLUS

CN Cyclosporin A, 4-[O-[4-[[[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-4'-yl)methyl]propylamino]-1,4-dioxobutyl]-N-methyl-L-threonine]- (9CI) (CA INDEX NAME)

PAGE 1-A

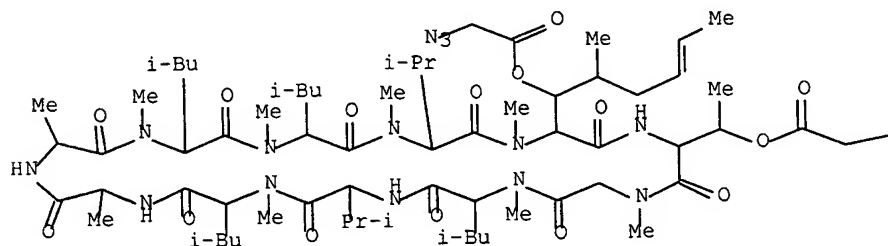


PAGE 1-B

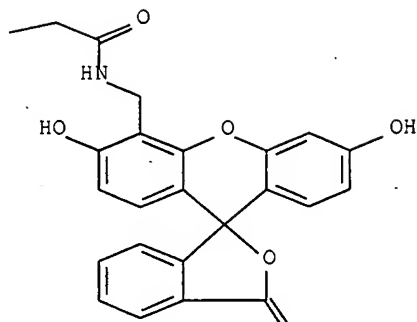


RN 141749-74-8 HCAPLUS  
 CN Cyclosporin A, 7-[O-[4-[[ (3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen)-4'-yl)methyl]amino]-1,4-dioxobutyl]-L-threonine]-, 6-(azidoacetate) (9CI) (CA INDEX NAME)

PAGE 1-A

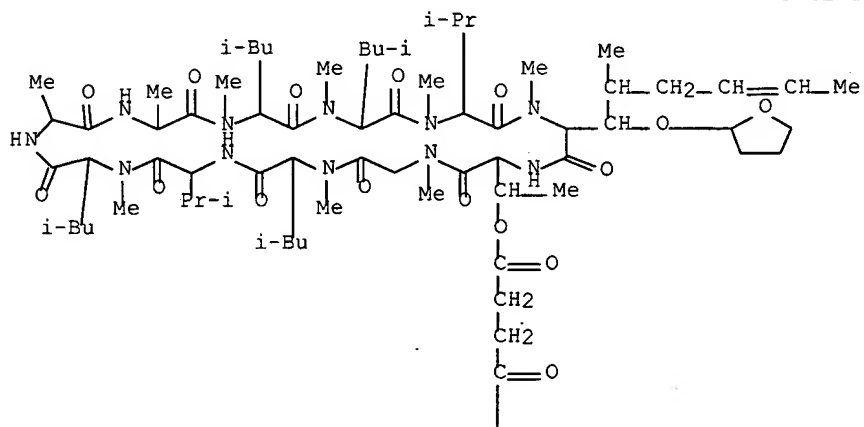


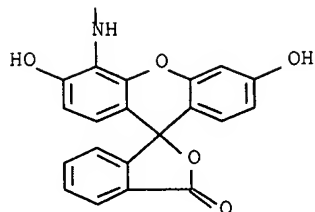




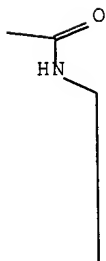
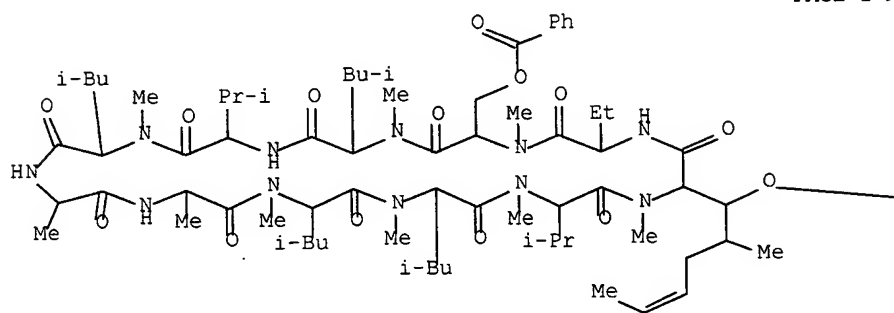
11

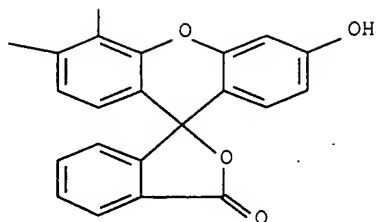
RN 141749-77-1 HCAPLUS  
 CN Cyclosporin A, 6-[(3R,4R,6E)-6,7-didehydro-N,4-dimethyl-3-[(tetrahydro-2-furanyl)oxy]-L-2-aminooctanoic acid]-7-[O-[4-[[[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen)-4'-yl)methyl]amino]-1,4-dioxobutyl]-L-threonine]- (9CI) (CA INDEX NAME)



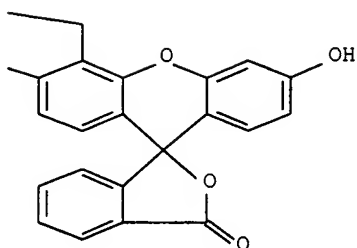
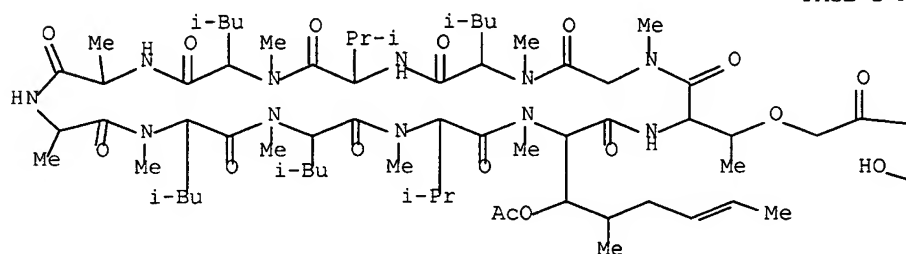


RN 141749-78-2 HCAPLUS  
 CN Cyclosporin A, 8-(O-benzoyl-N-methyl-L-serine)-, [(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-4'-yl)methyl]carbamate (ester) (9CI) (CA INDEX NAME)

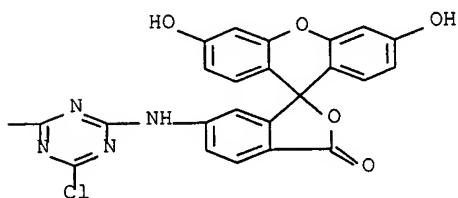
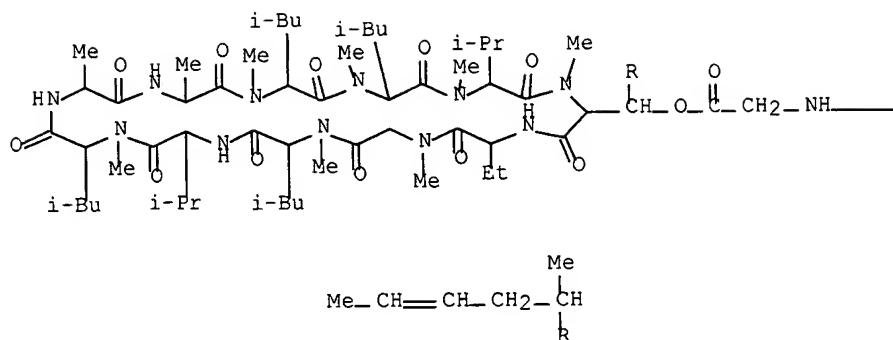




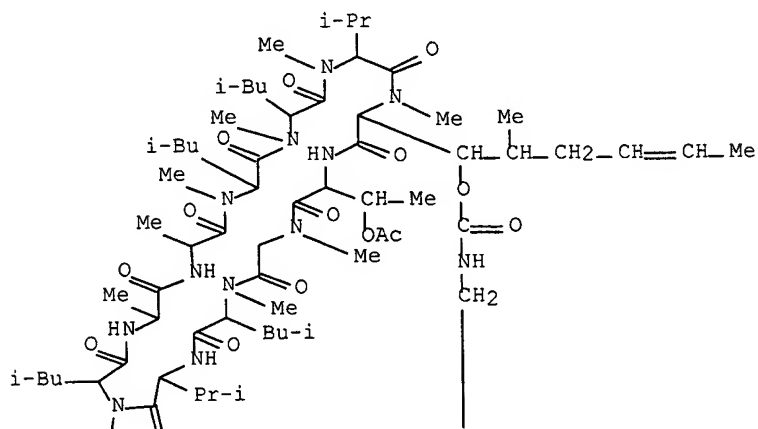
RN 141749-79-3 HCAPLUS  
 CN Cyclosporin A, 7-[O-[3-(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-4'-yl)-2-oxopropyl]-L-threonine]-, 6-acetate (9CI) (CA INDEX NAME)

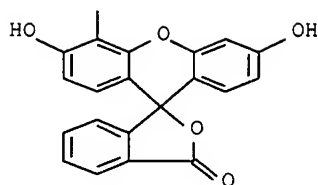
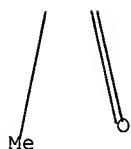


RN 141769-14-4 HCAPLUS  
 CN Cyclosporin A, ester with N-[4-chloro-6-[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)amino]-1,3,5-triazin-2-yl]glycine (9CI) (CA INDEX NAME)

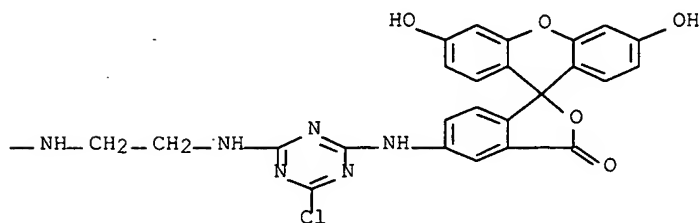
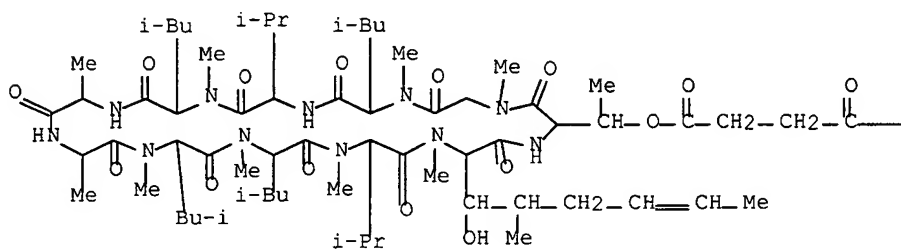


RN 141769-16-6 HCAPLUS  
 CN Cyclosporin A, 7-(O-acetyl-L-threonine)-, [(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-4'-yl)methyl]carbamate (ester) (9CI) (CA INDEX NAME)



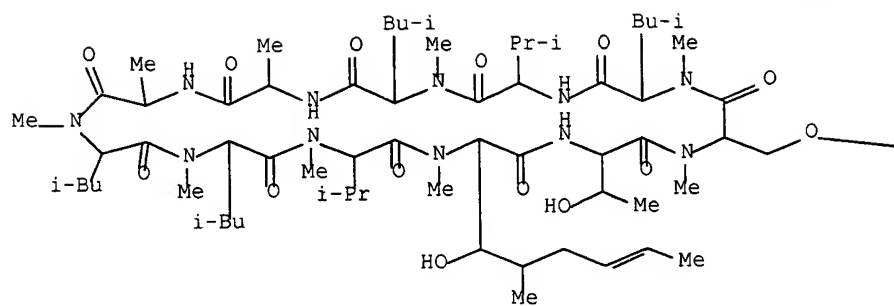


RN 141769-18-8 HCAPLUS  
 CN Cyclosporin A, 7-[O-[4-[[2-[[4-chloro-6-[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen)-6-yl]amino]-1,3,5-triazin-2-yl]amino]ethyl]amino]-1,4-dioxobutyl]-L-threonine]- (9CI) (CA INDEX NAME)



RN 141769-19-9 HCAPLUS  
 CN Cyclosporin A, 7-L-threonine-8-[O-[[[(3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen)-4'-yl)methyl]amino]carbonyl]-N-methyl-D-serine]- (9CI) (CA INDEX NAME)

PAGE 1-A



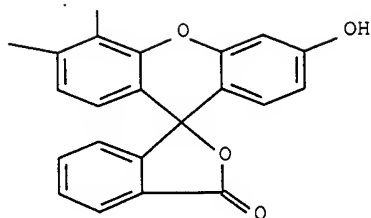
PAGE 1-B



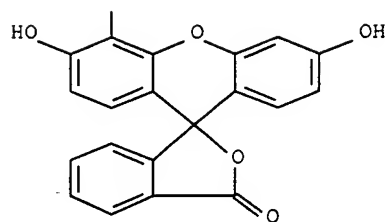
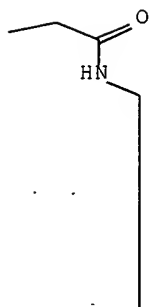
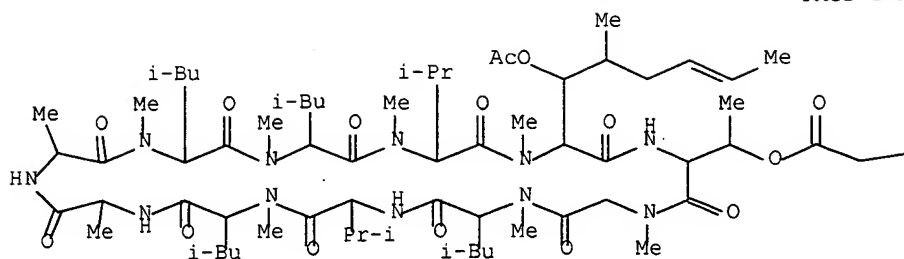
PAGE 2-A

HO\_

PAGE 2-B



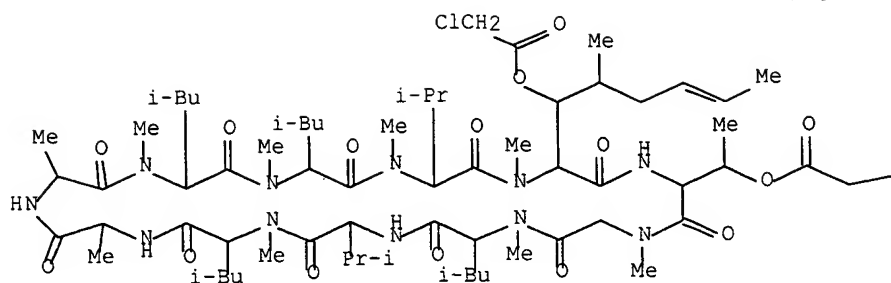
RN 141769-21-3 HCAPLUS  
CN Cyclosporin A, 7-[O-[4-[[[3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9']-[9H]xanthen]-4'-yl)methyl]amino]-1,4-dioxobutyl]-L-threonine]-, 6-acetate (9CI) (CA INDEX NAME)



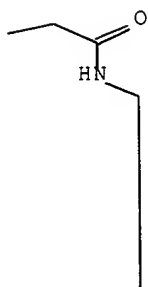
RN 141769-22-4 HCAPLUS

CN Cyclosporin A, 7-[O-[4-[[ (3',6'-dihydroxy-1-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen)-4'-yl)methyl]amino]-1,4-dioxobutyl]-L-threonine]-, 6-(chloroacetate) (9CI) (CA INDEX NAME)

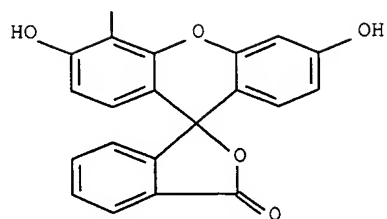
PAGE 1-A



PAGE 1-B

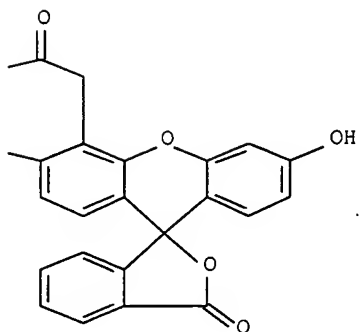
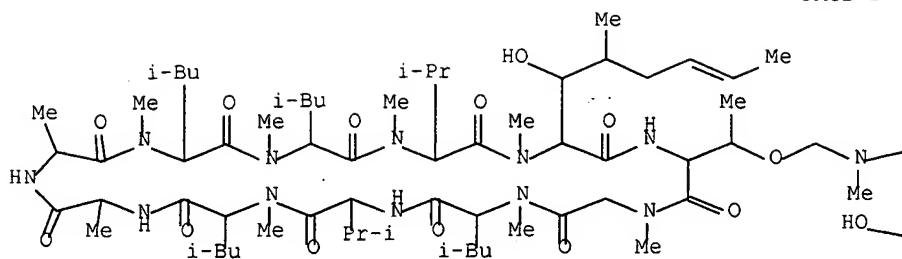


PAGE 2-B



RN 142064-94-6 HCAPLUS  
 CN Cyclosporin A, 7-[O-[[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-  
 [9H]xanthen]-4'-yl)acetyl]methylamino]methyl]-L-threonine]- (9CI) (CA  
 INDEX NAME)





RN 142123-01-1 HCAPLUS  
 CN Cyclosporin A, 6-ester with N-[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-6-yl)carbonyl]glycine (9CI) (CA INDEX NAME)

